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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/582,124

05/10/2007

Linda Greensmith

CytRx/012

1776

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ROPES & GRAY LLP
PATENT DOCKETING 39/361
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EXAMINER

STONE, CHRISTOPHER R

ART UNIT

PAPER NUMBER

1628

MAIL DATE

DELIVERY MODE

10/28/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/582,124	Applicant(s) GREENSMITH ET AL.	
	Examiner CHRISTOPHER R. STONE	Art Unit 1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 October 0209.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/08/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 8, 2009 has been entered.

Applicants' arguments, filed October 8, 2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Claims 6-11 are pending and under examination. Amyotrophic lateral sclerosis (ALS) is the elected specie of neurodegenerative disease currently under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kalmar et al (Experimental Neurology, Vol. 176, p. 87-97, 2002)

Claims 6-11 are drawn to a method of treating neurodegeneration in the central nervous system in a patient having ALS comprising administering (+)-R-N-[2-hydroxy-3-(1-piperidiny)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride or (+)-R-N-[2-hydroxy-3-(1-piperidiny)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate.

Kalmar et al teaches that (+)-R-N-[2-hydroxy-3-(1-piperidiny)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride (BRX-220) induces the expression of heat shock proteins (hsps), including hsp70 and hsp90, in motoneurons and surrounding cells, i.e. astrocytes, in the central nervous system (spinal cord, p. 89, Western Blots heading) and thus increases motoneuron and functional motor unit survival (i.e. treats neurodegeneration) following axotomy-induced cell death in neonatal rats (abstract). Heat shock proteins, including hsp70 and hsp90, are taught to provide cytoprotection of motor neurons (i.e. to treat neurodegeneration, p. 87, right column, 1st paragraph).

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Kalmar et al further teaches that the expression of said hsps may result in the astrocytic regulation and uptake of glutamate around the injured neurons, thereby decreasing the excitotoxic effects of glutamate. Said effects are taught to be a factor in the pathogenesis of ALS (p. 95, left column, line 40 to right column, line 34). Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of the instantly claimed invention to treat neurodegeneration in the central nervous system in a patient having ALS comprising administering BRX-220, since administration of the compound was taught to induce the expression of heat shock proteins in the central nervous system, said proteins were known to have cytoprotective effects on motoneurons in the central nervous system (i.e. to treat neurodegeneration), said proteins were also taught to likely inhibit the excitotoxic effects of glutamate and said effects were known to contribute to the pathogenesis of ALS, thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success. Additionally, it would have been prima facie obvious to one of ordinary skill in the art at the time of the instantly claimed invention to use (+)-R-N-[2-hydroxy-3-(1-piperidiny)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate, since the citrate salt form would have been reasonably expected to have the same or substantially the same therapeutic benefit as the free compound form.

Response to Arguments

Applicant alleges that no reference at the time of the filing of the instant application discloses the chemical identity of BRX-220 and thus one of ordinary skill in the art would have been motivated to use the compound in the instantly claimed invention. This is an allegation without factual support and is found unpersuasive

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because Kalmar et al provides motivation to use the compound in the instantly claimed method for the reasons noted above regardless of a potential lack of structural information about the compound. Applicant's arguments with regard to the salt form of the compound and Bruening et al are moot in view of the new grounds of rejection above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER R. STONE whose telephone number is (571)270-3494. The examiner can normally be reached on Monday-Thursday, 7:30am-4:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CRS

/Brandon J Fetterolf/
Primary Examiner, Art Unit 1642